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PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE, SUITE 1200
1201 PEACHTREE STREET
ATLANTA, GA 30361

EXAMINER	
LANDAU, SHARMILA GOLLAMUDI	
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JANE C. HIRSH, KAMAL K. MIDHA, MARK HIRSH, and WHE-YONG LO

Appeal 2007-3576
Application 09/858,016
Technology Center 1600

Decided: May 28, 2008

Before DONALD E. ADAMS, DEMETRA J. MILLS, and ERIC GRIMES, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 33-57, the only claims pending in this application. We have jurisdiction under 35 U.S.C. § 6(b).

INTRODUCTION

The claims are directed to a pharmaceutical composition (claims 33-54) and a process for the preparation of a pharmaceutical composition in unit dosage (claims 55-57). Claims 33, 41, and 55 are illustrative:

33. A pharmaceutical composition comprising:

(a) a first intraoral portion which rapidly dissolves or disintegrates intraorally to release a therapeutically effective amount of at least one pharmaceutically active ingredient which is capable of sublingual or buccal absorption through the mucous membranes of the mouth in a therapeutically effective level,

wherein the active ingredient is selected from the group consisting of Buprenorphine, Parecoxib, Aceclofenac, Buspirone, Ipsapirone, Fexofenadine, Loratadine, Dexbrompheniramine, Temelastine, Verapamil, Amlodipine, Ergotamine Tartrate, Dihydroergotamine, Ondansetron, Prochlorperazine, Sildenafil, Alprostadil, Sufentanil, Lofentanil, Carfentanil, Nalbuphine, Droperidol, and Haloperidol, being present in an amount between 1 micrograms [sic] and 50 mg, and having a rapid onset following intraoral administration, wherein the intraoral portion is a film coating that is applied to the core or a compression coating that is compressed around the core; and

(b) a second oral portion located within the first portion which contains a pharmaceutically active ingredient, which is released for uptake into the intestine in a therapeutically effective amount after the intraoral portion has disintegrated or dissolved, wherein the second portion is either a sustained release or chewable formulation.

41. A pharmaceutical composition comprising:

(a) a first intraoral portion which rapidly dissolves or disintegrates intraorally to release a therapeutically effective amount of at least one pharmaceutically active ingredient for uptake in the oral cavity in a therapeutically effective level,

the active ingredient having a molecular weight not exceeding 350 daltons or an active ingredient selected from the group consisting of Buprenorphine, Parecoxib, Aceclofenac, Buspirone, Ipsapirone, Fexofenadine, Loratadine, Dexbrompheniramine, Temelastine, Verapamil, Amlodipine, Ergotamine Tartrate, Dihydroergotamine, Ondansetron, Prochlorperazine, Sildenafil, Alprostadil, Sufentanil, Lofentanil, Carfentanil,

Nalbuphine, Droperidol, and Haloperidol, being present in an amount between 1 micrograms [sic] and 50 mg, and having a rapid onset following intraoral administration, wherein the intraoral portion is a film coating that is applied to the core or a compression coating that is compressed around the core;

(b) a pharmaceutically acceptable effervescent agent which generates effervescence or a pharmaceutically acceptable signaling system, located between the first intraoral component and the second oral component, that is detectable by the patient upon substantial release of the pharmaceutically active ingredient in the first intraoral component when contacted with salivary fluid; and

(c) a second oral portion located within the first portion which contains a pharmaceutically active agent, which is released for uptake into the intestine in a therapeutically effective amount after the intraoral portion has disintegrated or dissolved.

55. A process for the preparation of a pharmaceutical composition in unit dosage comprising

(a) a first intraoral portion which rapidly dissolves or disintegrates intraorally to release a therapeutically effective amount of at least one pharmaceutically active ingredient which is capable of sublingual or buccal absorption through the mucous membranes of the mouth in a therapeutically effective level,

wherein the active ingredient is selected from the group consisting of Buprenorphine, Parecoxib, Aceclofenac, Buspirone, Ipsapirone, Fexofenadine, Loratadine, Dexbrompheniramine, Temelastine, Verapamil, Amlodipine, Ergotamine Tartrate, Dihydroergotamine, Ondansetron, Prochlorperazine, Sildenafil, Alprostadil, Sufentanil, Lofentanil, Carfentanil, Nalbuphine, Droperidol, and Haloperidol, being present in an amount between 1 micrograms [sic] and 50 mg, and having a rapid onset following intraoral administration; and

(b) a second oral portion located within the first portion which contains a pharmaceutically active ingredient which is released for uptake into the intestine after the first intraoral portion has disintegrated or dissolved in a therapeutically effective amount after the intraoral portion has disintegrated or dissolved which comprises the steps of:

(i) providing the second oral component as an inner tablet core or as at least one layer of a multi-layer tablet core or as an uncoated capsule,

wherein the second oral component is either a sustained release or chewable formulation; and

(ii) applying the first intraoral component as an outer layer or as several outer layers forming an outer coating on the first portion, wherein the intraoral component is a film coating applied to the core or a compression coating compressed around the core.

The Examiner relies on the following prior art references to show unpatentability:

Sterling Drug Inc.	GB 800,973	Sep. 3, 1958
Fennell et al.	US 3,898,323	Aug. 5, 1975
Froemming	DE 33 38 978 A1	May 3, 1984
(Translation PTO 05-2823 April 2005)		
Lewis et al.	US 4,661,492	Apr. 28, 1987
Barclay et al.	US 5,053,032	Oct. 1, 1991
Jao et al.	US 5,310,561	May 10, 1994
Liedtke	US 5,686,112	Nov. 11, 1997
Johnson et al.	WO 00/35296	Jun. 22, 2000
Pather et al.	US 6,200,604 B1	Mar. 13, 2001
Neuser et al.	US 2001/0002999 A1	Jun. 7, 2001
Hirsh et al. (Hirsh 1)	US 6,863,901 B2	Mar. 8, 2005
Hirsh et al. (Hirsh 2)	US 2005/0123609 A1	Jun. 9, 2005[1]

Remington's Pharmaceutical Sciences 844 (18th ed.) (1990).

The rejections as presented by the Examiner are as follows:

1. Claims 33-40 and 55-57 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of the phrase "a second oral portion . . . which is released for uptake into the intestine . . . wherein the second portion is either a sustained release or chewable formulation".

[1] The Examiner refers to this document as "11/041474" (*see* Ans. 14).

2. Claims 33-57 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of the term "the core".

3. Claim 37 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of the phrase "comprises one or more of the outer layers".

4. Claims 33-39 and 41-56 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell.

5. Claims 41, 51, and 54 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Remington's, and Fennell.

6. Claims 33-36, 38-40, 42-44, 47, 48, 52, 53, 55, and 56 stand rejected under 35 U.S.C § 103(a) as unpatentable over Johnson.

7. Claim 57 stands rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Johnson and Jao.

8. Claims 33-36, 38, 39, 43, 44, 47-49, 52, 53, 55, and 56 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Neuser, Lewis and Liedtke.

9. Claims 33-43 and 49-57 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Barclay and Panther.

10. Claims 33-57 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of Hirsh 1.

11. Claims 33-57 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of Hirsh 2.

We affirm rejections 2, 4, 5, 8, 10, and 11. We reverse rejections 1, 3, 6, 7, and 9.

DISCUSSION

Findings of Fact (FF):

1. Sterling teaches

> [a] multi-layered pill or tablet particularly adapted for medicinal use and having a medicinal core and an intervening taste-indicating alarm layer or lamination, said indicating lamination having an outer medicinal layer which is soluble in the patient's mouth, to the end that the pill is held by the patient for absorption of the outer layer until the taste-indicating layer is exposed, the taste-indicating layer serving as an indication to the patient to swallow the tablet to obtain the benefits of gastro-intestinal absorption of the medicament within the pill or tablet; and the provision of a pill or tablet as above described including a plurality of layers, so that different or succeeding spaced dosages may be administered, the core being covered by an enteric coating, and in the event that a plurality of layers of medicament are provided within the taste-indicating layer, such multiple layers may each be covered enterically.

(Sterling 1: 11-31; *see generally* Ans. 4.)

2. Sterling teaches that the outer medicinal coating of the pill or tablet "is readily dissolved in the mouth" (Sterling 1: 59-61; Ans. 4).

3. Sterling teaches that the enteric layer "may be of a thickness to release the contained medicine at a definite point in the travel of the pill through the gastro-intestinal tract" (Sterling 1: 92 - 2: 4; Ans. 4).

4. Sterling's "invention provides a means for dosing a patient with at least two separate medicaments, one of which is to be absorbed in the mouth and the other in the gastro-intestinal tract" (Sterling 1: 47-51; Ans. 4).

5. Sterling exemplifies a tablet for the relief of asthma comprising an outer layer containing N-isopropylarterenol with an enteric layer comprising theophyllin and benzylephedrine (Sterling 2: 13-16; Ans. 4).

6. Sterling exemplifies a tablet for the relief of angina comprising an outer layer containing nitroglycerine with an enteric layer comprising pentaerithrytol tetranitrate (Sterling 2: 53-56; Ans. 4).

7. Sterling does not teach that the active ingredient is selected from the group consisting of Buprenorphine, Parecoxib, Aceclofenac, Buspirone, Ipsapirone, Fexofenadine, Loratadine, Dexbrompheniramine, Temelastine, Verapamil, Amlodipine, Ergotamine Tartrate, Dihydroergotamine, Ondansetron, Prochlorperazine, Sildenafil, Alprostadil, Sufentanil, Lofentanil, Carfentanil, Nalbuphine, Droperidol, and Haloperidol (Ans. 5) or the use of nitroglycerin at a concentration of 0.001 mg to 50 mg (Ans. 7).

8. Sterling teaches a shellac coating which is an enteric coating over the core (Sterling 2: 68-69; Ans. 22).

9. Sterling teaches the use of a flavor as a signal or alarm for the user to swallow the tablet (*see e.g.*, Sterling 2: 90-91). Sterling teaches that this signal may be "a layer between the outer medicament layer and the core" or "mixed throughout the outer medicament layer, so that then the disappearance of the alarm sensation serves as a signal for the patient to swallow the tablet" (Sterling 2: 86-91). In addition, Sterling teaches that the alarm layer may be on the interior of the tablet, or mixed with the interior medicament, so that its appearance is the signal (Sterling 2: 99-102).

10. Appellants' Specification discloses that a "chewable form comprises the pharmaceutically active ingredient capable of oral administration and pharmaceutically acceptable excipient for chewable tablets selected from the

group consisting of . . . starch . . . and magnesium stearate, optionally with a flavoring agent" (Spec. 25: 21-26). Sterling teaches tablet formulations wherein the core is formulated with starch and magnesium stearate (*see e.g.*, Sterling 2: 18-29).

11. Powell teaches vasopeptidase inhibitors to treat angina pectoris (Powell Abstract; Ans. 5).

12. Powell teaches the treatment of angina with one or more vasopeptidase inhibitors in combination with another class of pharmaceutically active agents known to be useful in the treatment of angina pectoris such as nitroglycerine, verapamil hydrochloride and amlodipine besylate (Powell 4: 6-16; Ans. 5).

13. Froemming teaches the cardiovascular therapeutic verapamil (Froemming 1: 1-4; Ans. 5).

14. Froemming teaches sublingual tablets and chewable capsules comprising 5-25 mg verapamil (Froemming 10: 17-18 and 11: 8-10; Ans. 5).

15. Froemming exemplifies a sublingual or buccal tablet comprising 20 mg of verapamil hydrochloride (Froemming 16: 1-3).

16. Fennell teaches a process for coating a tablet that comprises "tumbling the core in a drum containing the coating material or spray coating" or alternatively by applying the coating "over the tablet core by compressing the core with a tablet press" (Ans. 5; *see* Fennell 3: 14-26).

17. Remington's teaches that nitroglycerin has a molecular weight of 227.09 (Remington's 844: col. 1, l. 65; Ans. 7).

18. Remington's teaches that nitroglycerin is useful in the treatment of angina pectoris Remington's 844: col. 2).

19. Remington's teaches, *inter alia*, the use of nitroglycerin at a concentration of 1 mg for buccal administration (Remington's 844: col. 2, ll. 36-37).

20. Johnson teaches that "[o]ral administration of drugs is by far the most common method of moving drugs towards systemic circulation" and involves "the transport of cells [sic, drugs?] across the membranes of the epithelial cells within the gastrointestinal tract" (Johnson 2: 21-25).

21. Johnson teaches that a number of factors confound absorption after oral administration (Johnson 2: 25 - 3: 19).

22. Johnson teaches that parenteral administration is a non-preferred route of administration even though it eliminates a number of the variables associated with administering drugs orally (Johnson 3: 20-27).

23. Johnson teaches that there is "a need for an improved method of delivering drugs and other active agents to an individual" (Johnson 3: 28-29).

24. Johnson teaches a composition and method of making a medicinal chewing gum wherein the active agent is contained in the chewing gum coating and may also be present in the gum core (Johnson Abstract; Ans. 9).

25. Johnson teaches that the active agent may be applied to both the gum coating for fast release and also to the gum center with or without encapsulation for slow release (Johnson 15:9-12).

26. Johnson teaches that the active agent is added to the coating in a coating solution or premixed with a flavor or solvent (Johnson Abstract; Ans. 9).

27. Johnson teaches that "by adding the active agent to a gum coating, the medicament or active agent is quickly released from the chewing gum into saliva" (Johnson 4: 6-8; Ans. 9).

28. Johnson teaches that the active agent may be buspirone or verapamil (Johnson 11:25 - 12:2; Ans. 9).

29. Johnson teaches that

> [i]n contrast to a typically oral ingested drug, wherein the solution is in contact too briefly for absorption to be appreciable through the oral mucosa, it is believed that during the chewing, the active agent and/or medicament remains in the buccal cavity and may be forced or partitioned through the oral mucosa.

(Johnson 6:15-17).

30. Jao teaches a dosage form "provided as an osmotic device comprising a means for delivering an antiemetic drug at a controlled rate over time" (Jao 1: 14-18).

31. Jao's device can be manufactured to deliver an active agent through oral or sublingual and buccal routes (Jao 3: 66 - 4: 5).

32. Jao teaches the administration of ondansetron in an amount of 1 mg to 400 mg to the buccal mucosa for the treatment of nausea (Jao claim 4; Ans. 10).

33. Neuser teaches "medicinal preparations which can be administered orally and contain a fixed combination of at least one locally acting analgesic with a rapid onset of action and at least one systemically acting analgesic with a sustained action" (Neuser 1: ¶ 0001; Ans. 11).

34. Neuser teaches that the local analgesics are "rapidly acting and have an optimal duration of action lasting 0.5 to 120 minutes" (Neuser 1: ¶ 0013; Ans. 11).

35. Neuser teaches that the systemic analgesics "are those where a significant action has its onset after 15 minutes and lasts for up to 24 hours" and preferably "at least 3 hours" (Neuser 1: ¶¶ 0013 and 0015; Ans. 11).

36. Neuser teaches that the local analgesic may include lidocaine, prilocaine, mepivacaine, procaine and preferably benzocaine (Neuser 1: ¶¶ 0009 and 0014; Ans. 11).

37. Neuser teaches that the preparations may be formulated as "press-coated tablets, coated pastilles, chewing gum, hard carmel with liquid, semisolid or solid core. They are produced by conventional methods using customary ancillary substances" (Neuser 1: ¶ 0017; Ans. 11).

38. Neuser exemplifies a tablet comprising a core containing acetylsalicylic acid (ASA) or naproxen, orange juice flavoring, ascorbic acid, sucrose, microcrystalline cellulose, and saccharin; wherein the core is coated with a composition comprising benzocaine or lidocaine (Neuser 1: ¶¶0018-0021; Ans. 11).

39. Neuser does not teach the specific active agents recited in Appellants' claimed invention (Ans. 11).

40. Lewis teaches "[a]n analgesic composition in parenteral or sublingual unit dosage form comprising an active dose of buprenorphine" (Lewis Abstract; Ans. 11).

41. Lewis teaches an effective sublingual unit dosage of buprenorphine of "between about .01 to about 0.4 mg" (Lewis 2: 61-67; Ans. 11).

42. Lewis teaches that "[c]ompositions in the form of sublingual tablets contain soluble excipients such as lactose, mannitol, dextrose, sucrose, or mixtures thereof. They will also contain granulating and disintegrating agents such as starch, binding agents such as povidone or hydroxypropyl-methyl cellulose and lubricating agents such as magnesium stearate" (Lewis 4: 8-14).

43. Liedtke teaches that buprenorphine, lidocaine, prilocaine, and mepivacaine are known in the art as local anaesthetics (Liedtke 3: 1-9).

44. Barclay teaches "[a]n osmotic device for delivering a beneficial drug . . . into the mouth of a human patient" (Barclay Abstract; Ans. 12).

45. Barclay's

> device comprises a wall surrounding a compartment housing a layer of an agent that is insoluble to very soluble in aqueous biological fluids, e.g., saliva, and a layer of a fluid swellable, hydrophilic polymer. A passageway in the wall connects the agent with the exterior of the device. The wall is permeable to the passage of aqueous biological fluid but substantially impermeable to the passage of the hydrophilic polymer. The wall is sufficiently translucent to permit the patient to see the amount of drug/beneficial agent remaining to be delivered.

(*id.*).

46. Barclay teaches that

> "the device . . . can be used to extend the absorption period of a drug which might be poorly absorbed throughout certain portions of the GI tract, such as the colon. In such a case, it may be desirable to administer a predetermined percentage of a dose of the drug buccally followed by delivery of the remaining dose of drug in the device within the GI tract."

(Barclay 8: 28-35; Ans. 12.)

47. Barclay teaches a signaling means "in the form of a flavoring agent or coloring agent that alerts the patient that the buccal administration dosage has been delivered and the remainder may be swallowed" for delivery to the GI tract (Ans. 12; Barclay 3: 57 - 4: 2 and 5: 26-53).

48. Barclay teaches the use of, *inter alia*, prochlorperazine, nitroglycerine, ibuprofen, naproxen, and levodapa as suitable active agents (Ans. 12; Barclay 10: 50 - 11: 34).

49. Barclay teaches that the device can provide dosages of from about 0.05 ng to 500 mg or more of the drug, carrier, fillers, excipients, etc. (Ans. 12-13; Barclay 12: 22-24).

50. Barclay teaches the delivery of the active agent for an "extended period of time" or "extended delivery period" which "refers to periods greater than about 0.5 hours" (Barclay 15: 15-17; Ans. 13).

51. Pather teaches "[a] pharmaceutical dosage form adapted to supply a medicament to the oral cavity for buccal, sublingual or gingival absorption of the medicament which contains an orally administerable medicament in combination with an effervescent for use in promoting absorption of the medicament in the oral cavity" (Pather Abstract; Ans. 13).

52. Pather teaches that the effervescent is "used as [a] penetration enhancer to influence the permeability of the medicament across the buccal, sublingual, and gingival mucosa" (Pather 2: 6-10; Ans. 13).

53. Pather teaches that "effervescent compositions have also been employed for use as taste masking agents" (Panther 1: 29-30; Ans. 13).

54. Pather exemplifies the use of a 5 mg dosage of prochlorperazine for sublingual or buccal administration (Pather 6: 31 - 7: 9; Ans. 13).

55. Pather teaches that "[a]bsorption through the oral mucosa allows the drug to enter the systemic circulation without first passing through the liver" (Pather 3: 66 - 4: 2).

Definiteness:

1. Claims 33-40 and 55-57 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of the phrase "a second oral portion . . . which is released for uptake into the intestine . . . wherein the second portion is either a sustained release or chewable formulation".

The Examiner finds that claims 33 and 55 are directed, *inter alia*, "to a second oral portion which is released for uptake in the intestine and wherein the second portion is either a sustained release or chewable formulation" (Ans. 3). The Examiner finds that since the second oral portion is either a sustained release or chewable formulation it "unclear how the second oral portion is released in the intestine and yet is capable of being chewed" (*id.*). According to the Examiner, "if the second oral portion is chewed . . . the mastication process would cause the composition and the active to release in the mouth and not in the intestine" (Ans. 15). We note, however, that there is no evidentiary basis on this record to support this assertion.

As Appellants point out "[c]hewable does not mean that release must occur in the mouth" (Reply Br. 3). According to Appellants, "[r]elease is generally interpreted as well [sic] the drug is released in a form suitable for uptake" (*id.*). "In this case, chewing breaks up drug containing particles, which are swallowed and pass into the small intestine, where uptake occurs" (*id.*).

We find that Appellants have the better argument. Accordingly, we reverse the rejection of claims 33-40 and 55-57 under 35 U.S.C. § 112, second paragraph.

2. Claims 33-57 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of the term "the core".

The Examiner finds that there is insufficient antecedent basis for the term "the core" as it appears in claims 33, 41, and 55 (Ans. 4). Claims 34-40, 42-54, 56, and 57 depend directly from claims 33, 41, or 55. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Therefore, we limit our discussion to representative claim 33.

Appellants assert that while they believe the claims are clear and fully supported as presented, they will amend the claims "to define a core or to define the intraoral portion as a film coating or compression coating which is applied to the second oral portion" (App. Br. 6); or "as required by the Examiner to provide antecedent basis" (Reply Br. 4).

Claim 33 requires, *inter alia*, that the first intraoral portion is a film coating that is applied to the core or a compression coating that is compressed around the core. Upon consideration of claim 33, we find no limitation that defines the composition as comprising a "core". Therefore, we agree with the Examiner that the recitation of the term "the core" in claim 33 is indefinite. Accordingly, we affirm the rejection of claim 33 under 35 U.S.C. § 112, second paragraph. Claims 34-57 fall together with claim 33.

3. Claim 37 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of the phrase "comprises one or more of the outer layers".

The Examiner finds that there is insufficient antecedent basis for the phrase "comprises one or more of the outer layers" as it appears in claim 37 (Ans. 4).

In response, Appellants assert that

> [c]laim 37 depends from claim 35, which defines the composition of claim 33 in the form of a tablet or capsule unit dosage form. Claim 37 defines the tablet of claim 33 as a multilayer tablet, wherein the oral component comprises one or more inner layers of the tablet and the intraoral component comprises one or more outer layers of the tablet.

(App. Br. 6-7.) Accordingly, Appellants assert that "[t]he antecedent basis is inherent in the claim itself" (App. Br. 7; Reply Br. 4). We agree.

Claim 37 ultimately depends from claim 33 and further limits claim 33 to a pharmaceutical composition that is in a tablet or capsule unit dosage form, wherein the unit dosage form is a multi-layer tablet wherein the second oral portion of the composition comprises one or more inner layers of the tablet and the first intraoral component comprises one or more of the outer layers of the multi-layer tablet.

We are not persuaded by the Examiner's intimation that claim 37 is indefinite simply because Appellants use the term "the" when they refer to "*the* outer layers of the multi-layer tablet" (Ans. 16). The legal standard for indefiniteness under 35 U.S.C § 112, second paragraph, is whether a claim reasonable apprises those of skill in the art of its scope. *See, Amgen Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1217 (Fed. Cir. 1991).

We find that claim reads, *inter alia*, on a tablet or capsule unit dosage form that has multiple layers, wherein the second oral portion comprises one or more inner layers and the first intraoral component comprises one or more outer layers of the multi-layer tablet.

Accordingly, we reverse the rejection of claim 37 under 35 U.S.C. § 112, second paragraph.

Obviousness:

Notwithstanding the foregoing indefiniteness issue with regard to the term "the core", for the purposes of the prior art rejections we will interpret claim 33 to read on a composition that comprises a core.

4. Claims 33-39, 41-50, and 51-56 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell.

Based on the combination of references relied upon, the Examiner concludes that

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the teachings of Powell and utilize the instant verapamil in [Sterling's] nitroglycerine example. One would have been motivated to do so since Powell teaches that the prior art's nitroglycerin and . . . verapamil are both utilized to treat angina. Thus, a skilled artisan would have been motivated to substitute nitroglycerin with verapamil with the expectation of similar results since [Sterling] teaches the use of nitroglycerine to promptly treat angina and the prior art teaches that both drugs treat angina.

(Ans. 5.) In addition, the Examiner reasons that a person of ordinary skill in the art at the time the invention was made would have formulated the tablet with 5-25 mg of verapamil in a sublingual/buccal tablet as taught by Froemming (Ans. 5-6). According to the Examiner a person of ordinary skill in the art at the time the invention was made would have expected success in utilizing verapamil in Sterling's formulation since Sterling "teaches the only criticality of the medicament in the first layer is that it must be capable of being absorbed in the mouth and [Froemming] demonstrates [that] verapamil satisfies this requirement; i.e. it is capable of being absorbed buccally or sublingually" (Ans. 6).

With regard to the application of the coating as a film coating or by compression coating, the Examiner finds that Fennell teaches various coating methods including compression coating and tumble coating as taught by Sterling (Ans. 6). Accordingly, the Examiner concludes that "a skilled artisan would have expected [similar] results by utilizing a coating compression rather than the method taught by [Sterling] since Fennell teaches both manners are conventionally known and utilized for coating cores" (*id.*). We find no error in the Examiner's prima facie case of obviousness.

Appellants present arguments that correspond to the following claim groupings: I. claims 33, 35, 36, 38, 39, 42, 49, 51, 52, and 54; II. claim 34; III. claim 37; IV. claims 41 and 50; V. claims 43 and 44; VI. claims 45 and 46; VII. claim 47; VIII. claim 48; IX. claim 53; and X. claims 55 and 56. Accordingly, we limit our discussion to claims 33, 34, 37, 41, 43, 45, 47, 48, 53, and 55. 37 C.F.R. § 41.37(c)(1)(vii).

Claim 33:

According to Appellants "[n]one of the prior art teaches the desirability of a single formulation providing release at two sites and times: intraoral (first) and oral (second)" (App. Br. 12). We disagree. Sterling teaches a single formulation that provides a means for dosing a patient with at least two separate medicaments, one of which is to be absorbed in the mouth and the other in the gastro-intestinal tract (FF 1 & 4).

Appellants assert that Sterling fails to disclose a "pharmaceutical composition comprising a first intraoral portion which rapidly dissolves or disintegrates intraorally to release a therapeutically effective amount of at least one pharmaceutically active ingredient which is absorbed through the buccal or sublingual mucosa . . . for uptake in the oral cavity in a therapeutically effective level" (App. Br. 12). We disagree, *see* FF 1-6.

According to Appellants, Sterling's disclosure of delayed release is not the same as sustained release because Appellants believe that "[s]ustained release is where the drug is released over an extended period of time, for example 0.5 to 24 hours ([Specification] page 23, lines 21-26)" (App. Br. 13). We are not persuaded.

A preferred embodiment of Appellants' invention is the sustained release of a drug over a period of from 0.5 to 24 hours (Spec. 23: 21-26). Claim 33 sets no time period for the release of the drug. As the Examiner points out, "the term 'sustained' is a relative term and any time frame can read on it" (Ans. 23). In this regard, the Examiner explains that "Sterling teaches a shellac coating . . . which is an enteric coating over the core" (Ans. 22; FF 8). Absent evidence to the contrary, of which there is none of record, a person of ordinary skill in the art would expect that the drug formulated in

the shellac coating of Sterling's core would not all be released at the same time. Accordingly, Sterling's shellac coated drug containing core reads on a sustained release formulation within the scope of Appellants' claimed invention. Accordingly, we are not persuaded by Appellants' assertion to the contrary.

Appellants assert that there is "no motivation for a skilled artisan to combine Fennell with Sterling. The mere fact that Fennell discloses that the tablet can be coated with the alkaline material as a film or compressed thereon, does not provide one of ordinary skill in the art with a reason to combine Fennell with Sterling" (App. Br. 13). We disagree. Fennell teaches a number of processes for formulating a tablet which include applying a coating over the tablet core by compressing the core with a tablet press (FF 16). There is no evidence on this record that would suggest that the tablet taught by the combination of references could not be coated by the use of compression as taught by Fennell. Further contrary to Appellants' assertion the Examiner has explained that "a skilled artisan would have expected [similar] results by utilizing a coating compression rather than the method taught by [Sterling] since Fennell teaches both manners are conventionally known and utilized for coating cores" (Ans. 6). Accordingly, we are not persuaded by Appellant's assertion.

We also disagree with Appellants' assertion that the Examiner's reliance on Froemming and Powell is based on hindsight reconstruction of Appellants' claimed invention (App. Br. 13). As the Examiner explains Powell teaches that nitroglycerin and verapamil are both useful in the treatment of angina (Ans. 5; FF 12). Sterling teaches a formulation for the treatment of angina that utilized nitroglycerin (FF 6). Where, as here, the

prior art recognizes two components to be equivalent, an express suggestion to substitute one for another need not be present in order to render such substitution obvious. *In re Fout*, 675 F.2d 297, 301 (CCPA 1982). As to Froemming, the Examiner found that verapamil is useful as a cardiovascular therapeutic (FF 13). Therefore, one utilizing verapamil would consider Froemming and realize that verapamil is an effective sublingual or buccal agent at a dosage range of 5-25 mg (FF 14 and 15). Accordingly, we are not persuaded by Appellants' assertion.

For the foregoing reasons we are not persuaded by Appellants' assertion that the Examiner's focus on Powell and Froemming is irrelevant to the claimed invention "since the missing and critical element is the selection of a drug which is released and taken up sublingually, placed on the outside of a formulation which is swallowed and subsequently absorbed from the small intestine" (Reply Br. 6). As discussed above, this "critical element" is taught by Sterling (FF 1-4).

For the foregoing reasons we affirm the rejection of claim 33 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell. Claims 35, 36, 38, 39, 42, 49, 51, 52, and 54 fall together with claim 33.

Claim 34

Claim 34 depends from and further limits the active ingredient of claim 33 to one that would otherwise undergo first pass metabolism.

Appellants assert that "[n]one of the cited art discloses or leads one to select the intraoral component of a two component system as one which would otherwise undergo first pass metabolism" (App. Br. 17). For the

reasons set forth above, the combination of prior art relied upon by the Examiner would have led one of skill in the art to select verapamil for the treatment of angina. There is no evidence on this record that this compound would not otherwise undergo first pass metabolism. Accordingly, we are not persuaded by Appellants' assertion to the contrary and the rejection of claim 34 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell is affirmed.

Claim 37:

Claim 37 depends ultimately from and further limits claim 33 to a tablet unit dosage form, wherein the second oral portion of the composition is an inner core of the tablet surrounded by an outer coating of the first intraoral component.

According to Appellants "[n]one of the cited art discloses multilayer tables [sic] with multiple layers of an intraoral and/or oral component" (App. Br. 17). We disagree, *see* FF 1.

Accordingly, we are not persuaded by Appellants' assertion to the contrary and the rejection of claim 37 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell is affirmed.

Claim 41:

Appellants assert that "[c]laim 41 differs from claim 33 by requiring that the drug to be delivered intraorally is either as listed in claim 33 or has a molecular weight not exceeding 350 daltons, and requires either an effervescence or pharmaceutically acceptable signaling system between the

two components" (App. Br. 17). Other than identifying the differences between claims 33 and 41 Appellants have not identified an error in the Examiner's prima facie case of obviousness.

Since Appellants fail to identify an error in the Examiner's prima facie case of obviousness, we affirm the rejection of claim 41 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell. Claim 50 falls together with claim 41.

Claim 43:

Claim 43 depends from and further limits claim 33 to require that the second oral component is in a sustained release formulation.

Appellants assert that "[d]elayed release which is taught by Sterling, is not the same as sustained release" (App. Br. 19). Thus, Appellants conclude that "[n]one of the cited art discloses a second component in a two component formulation which provides sustained release" (*id.*). For the reasons set forth above we disagree.

Accordingly, we affirm the rejection of claim 43 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell. Claim 44 falls together with claim 43.

Claim 45:

Claim 45 depends from and further limits claim 33 to comprise a delayed release coating. According to Appellants "[n]one of the cited art discloses a two component system wherein the second component is for oral delivery and provides for delayed release" (App. Br. 19). For the foregoing reasons we disagree.

Accordingly, we affirm the rejection of claim 45 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell. Claim 46 falls together with claim 45.

Claim 47:

Claim 47 depends from and further limits the second oral component of claim 33 to one that is chewable and comprises at least one pharmaceutically acceptable excipient suitable for a chewable medication and a flavoring agent.

According to Appellants "[n]one of the cited art discloses a pharmaceutical composition with two portions wherein the second portion is chewable, and comprises at least one pharmaceutically acceptable excipient suitable for a chewable medication and a flavoring agent" (App. Br. 19). We disagree. *See* FF 10. Accordingly, we are not persuaded by Appellants' assertion that the prior art relied upon fails to teach a second oral component that contains a flavoring agent.

Regarding a chewable second portion, the Examiner explains that "Sterling's core comprises excipients that are capable of being chewed" (Ans. 24). In this regard, the Examiner "points out that page 25, lines 20-25 of the instant disclosure states, 'pharmaceutically acceptable excipient for chewable tablets selected from the group consisting of . . . starch . . . magnesium stearate, optionally with a flavoring agent' . . . Sterling teaches starch and magnesium stearate in the core composition" (*id.* (emphasis removed)). Therefore, the Examiner concludes that Sterling's "core is capable of being chewed and contains 'chewable excipients'" (*id.*). We find no error in the Examiner's reasoning.

As Appellants point out "[a]ll tablets are capable of being chewed" (Reply Br. 12 (emphasis removed)). Nevertheless, Appellants assert that

> [o]ne of ordinary skill in the art understands that chewable formulations are formulations that are meant to be chewed and would recognize that this would affect not only the excipients included in the formulation, but the combination of excipients and for a particular excipient, the concentration, depending on its intended use in the formulation.

(*Id.*) Appellants do not, however, direct our attention to any evidence on this record that supports this position. The evidence on this record does, however, support the Examiner's position. *See* FF 10.

While Appellants assert that a particular concentration of excipients is required, Appellants fail to direct our attention any description in their Specification or claims that require a particular excipient concentration for their chewable formulation. Therefore, we find that the preponderance of the evidence on this record falls in favor of the Examiner. Accordingly, we affirm the rejection of claim 47 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell.

Claim 48:

Claim 48 depends from and further limits claim 33 to require that the first intraoral component disintegrates or dissolves within 10 minutes, when the composition is contacted with saliva during intraoral administration.

According to Appellants "[t]he examiner has cited no art teaching the criticality of a two component system wherein the first component dissolves or disintegrates within 10 minutes, nor where the second component must remain intact after the first component is delivered" (App. Br. 20). We

disagree. First, Sterling teaches that the outer medicinal coating of the pill or tablet is readily dissolved in the mouth (FF 2). The teaching that the coating is "readily dissolved" is reasonably interpreted to mean it dissolves within 10 minutes. There is no evidence on this record to suggest that Sterling's outer medicinal coating will not dissolve or disintegrate within 10 minutes, when the composition is contacted with saliva during intraoral administration. Second, contrary to Appellants' assertion there is no requirement in claim 48 that the second component must remain intact after the first component is delivered. Accordingly, we are not persuaded by Appellants' arguments.

Therefore, we affirm the rejection of claim 48 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell.

Claim 53:

Claim 53 depends from and further limits the active ingredient in the first intraoral composition of claim 33 to a dosage of between 10 micrograms and 30 mg.

According to Appellants "[t]he examiner has cited no art disclosing the claimed dosage range of one to 50 mg, much less the claimed range of 10 to 30 mg of claim 53, for a drug to be delivered intraorally" (App. Br. 20). We disagree, *see* FF 13-15.

Accordingly, we are not persuaded by Appellants' assertion to the contrary and the rejection of claim 53 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell is affirmed.

Claim 55:

Appellants assert that

> [t]he same arguments made with respect to the formulations are equally applicable here. Sterling does not disclose a process for preparing a pharmaceutical composition in unit dosage, comprising two portions wherein the first is an intraoral portion which disintegrates to release a pharmaceutically effective amount of at least one active ingredient which is absorbed intraorally due to the chemical composition and dosage and a second portion which is released and absorbed within the lower gastrointestinal tract from either a sustained release or chewable formulation.

(App. Br. 20.) We disagree, *see* FF 1-6. Appellants make no other argument with regard to the Examiner's prima facie case of obviousness. Accordingly we affirm the rejection of claim 55 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Powell, Froemming, and Fennell. Claim 56 falls together with claim 55.

5. Claims 41, 51, and 54 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Remington's, and Fennell.

These claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Therefore, we limit our discussion to representative claim 41.

Based on the combination of references relied upon the Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the teachings of Remington's and utilize the concentration set forth therein to formulate a medicament for the treatment of angina (Ans. 8).

With regard to the application of the coating as a film coating or by compression coating, the Examiner finds that Fennell teaches various coating methods including compression coating and tumble coating as taught by Sterling (Ans. 8). Accordingly, the Examiner concludes that "a skilled artisan would have expected [similar] results by utilizing a coating compression rather than the method taught by [Sterling] since Fennell teaches both manners are conventionally known and utilized for coating cores" (*id.*). We find no error in the Examiner's prima facie case of obviousness.

Appellants do not dispute that Remington's teaches "that nitroglycerin has a molecular weight of 227.09 and that the dose of nitroglycerin is between 1 mg and 0.15-0.6 mg for buccal tablets and sublingual tablets, respectively" (App. Br. 21; *see also* FF 17-19).

Appellants assert that "Sterling does not disclose a pharmaceutical composition comprising a pharmaceutically acceptable . . . signaling system, located between a first intraoral component and a second oral component" (*id.*). We disagree, *see* FF 1-4.

Appellants assert that "Sterling also does not disclose a composition where the intraoral portion is . . . a compression coating compressed around the core" (App. Br. 21). This is, however, why the Examiner relied upon Fennell. Nevertheless, Appellants assert that there is no motivation to combine Sterling and Remington's with Fennell because "Fennell does not disclose or suggest coating a composition containing an intraoral component and an oral component as defined in claim[ ] 41" (App. Br. 22). While this may be true, Appellants have not articulated a reason why one of ordinary skill in the art would not have utilized Fennell's compression coating

methodology in the formulation of Sterling's tablet. As discussed above, the Examiner explained that "a skilled artisan would have expected [similar] results by utilizing a compression coating rather than the method taught by [Sterling] since Fennell teaches both manners are conventionally known and utilized for coating cores" (Ans. 8). Appellants provide no persuasive argument or evidence to rebut this point.

Accordingly, we affirm the rejection of claim 41 under 35 U.S.C § 103(a) as unpatentable over the combination of Sterling, Remington's, and Fennell. Claims 51 and 54 fall together with claim 41.

6. Claims 33-36, 38-40, 42-44, 47, 48, 52, 53, 55, and 56 stand rejected under 35 U.S.C § 103(a) as unpatentable over Johnson.

The claims require, *inter alia*, that the second oral portion contains a pharmaceutically active ingredient, which is released for uptake into the intestine in a therapeutically effective amount after the first intraoral portion has disintegrated or dissolved. In contrast, Johnson teaches that the active agent remains in the buccal cavity where it is absorbed through the oral mucosa (FF 29). In this regard, Johnson distinguishes between the delivery of an active agent that is absorbed through the gastrointestinal tract from those that are delivered to the buccal cavity and absorbed through the oral mucosa (FF 20, 21, 23, and 29). The Examiner does not identify, and we do not find, a teaching in Johnson of an active agent that is released for uptake into the intestine in a therapeutically effective amount after the first intraoral portion has disintegrated or dissolved.

Accordingly, we reverse the rejection of claims 33-36, 38-40, 42-44, 47, 48, 52, 53, 55, and 56 under 35 U.S.C § 103(a) as unpatentable over Johnson.

7. Claim 57 stands rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Johnson and Jao.

The Examiner relies on Johnson to teach method of making a chewing gum wherein an active agent is contained in the gum core and in the coating (Ans. 9). The Examiner relies on Jao to teach the administration of "ondansetron in an amount of 1 mg to 400 mg to the buccal mucosa for the treatment of nausea" (FF 32). Based on this evidence the Examiner finds that

> [i]t would have been obvious for one of ordinary skill in the art at the time the invention was made to utilize ondansetron in Johnson's gum coating. One would have been motivated to do so if one wanted to treat nausea. Further, one would have expected success since Johnson teaches the gum coating contains an active that administers the drug to the buccal mucosa.

(Ans. 10.)

In response, Appellants assert that

> Johns[on] describes chewing gums, not capsules or tablets. Jao describes a dosage form containing a wall that surrounds a lumen comprising the drug, a driving means for delivering the drug, and a rate controlled exit means. One of ordinary skill[ ] in the art would not be motivated to combine the chewing gums of Johnson with the dosage form described in Jao. The references, in combination, do not disclose each and every element of claim 57 nor the motivation to combine.

(App. Br. 22.) We agree.

While the Examiner emphasizes that Johnson's "chewing gum reads on [a] 'tablet'", the Examiner also emphasizes that Jao is relied upon solely "to teach the instant drug ondansetron . . . and not the dosage form since Johnson is not deficient in this sense" (Ans. 31). We disagree with this analysis.

Contrary to the Examiner's assertion Johnson fails to teach an active agent that is released for uptake into the intestine in a therapeutically effective amount. The Examiner's reliance on Jao to teach the administration of "ondansetron in an amount of 1 mg to 400 mg to the buccal mucosa for the treatment of nausea" (FF 32; Ans. 31) fails to make up for the deficiency in Johnson. Further, while Jao teaches oral administration of the drug, which presumably will result in administering the active agent for uptake into the intestine in a therapeutically effective amount, the Examiner fails to articulate how a person of ordinary skill in the art would combine Johnson's chewing gum with Jao's device or incorporate Jao's device in Johnson's method of preparing a medicated chewing gum.

Accordingly, we reverse the rejection of claim 57 under 35 U.S.C § 103(a) as unpatentable over the combination of Johnson and Jao.

8. Claims 33-36, 38, 39, 43, 44, 47-49, 52, 53, 55, and 56 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Neuser, Lewis and Liedtke.

Based on the combination of references relied upon the Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Neuser and Lewis, and substitute Neuser's anaesthetics with buprenorphine (Ans. 11).

The Examiner reasons that since Liedtke teaches the anaesthetics taught by Neuser and buprenorphine function as local anesthetics, one of ordinary skill in the art would have been motivated to make the substitution since Lewis teaches the analgesic effects of buprenorphine in a sublingual tablet form (Ans. 11-12). According to the Examiner "a skilled artisan would have expected similar results and success by substituting the prior art's anaesthetic with buprenorphine since the prior art establishes the functional equivalency" (Ans. 12). We find no error in the Examiner's prima facie case of obviousness.

Appellants present arguments that correspond to the following claim groupings: I. claims 33, 35, 36, 38, 39, 49, and 52; II. claim 34; III. claims 43 and 44; IV. claim 47; V. claim 48; VI. claim 53; VII. claims 55 and 56.

Claim 33:

According to Appellants "Buprenorphine is a long acting drug" and therefore, "[o]ne of ordinary skill in the art would . . . not have [been] motivated to substitute Neuser's anesthetics with buprenorphine as asserted by the Examiner" (App. Br. 14).

Claim 33 does not, however, require the active agent to be long or short acting, it only requires that the active agent have rapid onset following intraoral administration. Appellants fails to identify any evidence on this record to suggest that buprenorphine would not have rapid onset following intraoral administration. Further, while Neuser teaches that the local analgesics are rapid acting, Neuser does not require the local analgesics to be short or long acting. As the Examiner explains Neuser discloses that an optimal duration of the local analgesic is 0.5 to 120 minutes (Ans. 33; FF

34). In this regard, the Examiner explains that Neuser identifies a number of active agents that are suitable as a local analgesic, including "[m]epivacaine [which] has a duration of 2-3 hours and bupivacaine [which] has a duration of 3-5 hours" (Ans. 33; FF 36).

Appellants also assert that "buprenorphine does not have a rapid onset of action as required by Neuser" (Reply Br. 13). In this regard, Appellants assert that "[b]uprenorphine has an onset of action of 60-120 minutes" and "Neuser teaches away from analgesics which have an onset of action longer than 10 minutes" (Reply Br. 14). Appellants fail to support these assertions with evidence on the record. Further, Appellants fail to provide an evidentiary basis to support the intimation that buprenorphine would not have a rapid onset of action within the scope of Neuser when administered sublingually or buccally. In this regard, we direct attention to Lewis, which teaches a sublingual or buccal formulation comprising buprenorphine (FF 40). In addition, Appellants' assertion is contrary to Appellants' claimed invention, which requires, *inter alia*, that buprenorphine have rapid onset following intraoral administration. Accordingly, we are not persuaded by this unsupported and contradictory assertion.

We also recognize Appellants' assertion that Liedtke discloses topical not oral formulations (App. Br. 14; Reply Br. 14). We are not persuaded. The Examiner relies on Liedtke simply to show that the active agents taught by the combination of references relied upon were known in the art as local anaesthetics at the time the invention was made (FF 43; Ans. 33).

For the foregoing reasons, we find that the preponderance of the evidence of record falls in favor of the Examiner. Accordingly, we affirm the rejection of claim 33 under 35 U.S.C § 103(a) as unpatentable over the

combination of Neuser, Lewis and Liedtke. Claims 35, 36, 38, 39, 49, and 52 fall together with claim 33.

Claim 34:

Claim 34 depends from and further limits the active ingredient of claim 33 to on that would otherwise undergo first pass metabolism.

Appellants assert that "[n]one of the cited art discloses or leads one to select the intraoral component of a two component system as one which would otherwise undergo first pass metabolism" (App. Br. 17). For the reasons set forth above, the combination of prior art relied upon by the Examiner leads one to select buprenorphine as a local analgesic in Neuser's formulation. There is no evidence on this record that this compound would not otherwise undergo first pass metabolism. Accordingly, we are not persuaded by Appellants' assertion to the contrary and the rejection of claim 34 under 35 U.S.C § 103(a) as unpatentable over the combination of Neuser, Lewis and Liedtke is affirmed.

Claim 43 and 44:

Claim 43 depends from and further limits claim 33 to require that the second oral component is in a sustained release formulation. Appellants assert that "[n]one of the cited art discloses a second component in a two component formulation which provides sustained release" (App. Br. 19).

Appellants' Specification describes a delayed release formulation that preferably "lasts 0.5 to 12 hours" wherein the delayed release coating may be any number of cellulose derived compounds (Spec. 27: 18 - 28: 2). Appellants fail to explain why the core of Neuser's formulations would not

be expected to produce a delayed release formulation within the scope of Appellants' claimed invention (*see* FF. 37 and 38). Accordingly, we are not persuaded by Appellants' assertion to the contrary.

Accordingly, we affirm the rejection of claim 43 under 35 U.S.C § 103(a) as unpatentable over the combination of Neuser, Lewis and Liedtke. Claim 44 falls together with claim 43.

Claim 47:

Claim 47 depends from and further limits the second oral component of claim 33 to one that is chewable and comprises at least one pharmaceutically acceptable excipient suitable for a chewable medication and a flavoring agent.

According to Appellants "[n]one of the cited art discloses a pharmaceutical composition with two portions wherein the second portion is chewable, and comprises at least one pharmaceutically acceptable excipient suitable for a chewable medication and a flavoring agent" (App. Br. 19). We disagree.

Neuser teaches a two component analgesic preparation (FF 33) that may be formulated to be chewable (FF 37), comprises a core that contains a systemic analgesic and a flavoring agent (FF 38), and a local analgesic that is present as a coating on the core of the tablet (*id.*). Accordingly, we are not persuaded by Appellants' argument.

Therefore, we affirm the rejection of claim 47 under 35 U.S.C § 103(a) as unpatentable over the combination of Neuser, Lewis and Liedtke.

Claim 48:

Claim 48 depends from and further limits claim 33 to require that the first intraoral component disintegrates or dissolves within 10 minutes, when the composition is contacted with saliva during intraoral administration.

According to Appellants "[t]he examiner has cited no art teaching the criticality of a two component system wherein the first component dissolves or disintegrates within 10 minutes, nor where the second component must remain intact after the first component is delivered" (App. Br. 20). We disagree. First, contrary to Appellants' assertion there is no requirement in claim 48 that the second component must remain intact after the first component is delivered. Second, Lewis teaches that "[c]ompositions in the form of sublingual tablets contain soluble excipients such as lactose, mannitol, dextrose, sucrose, or mixtures thereof. They will also contain granulating and disintegrating agents such as starch, binding agents such as povidone or hydroxypropyl-methyl cellulose and lubricating agents such as magnesium stearate" (FF 42). There is no evidence on this record that such a composition could not be coated onto Neuser's tablet core and that in doing so that such a coating would not disintegrate or dissolve within 10 minutes, when the composition is contacted with saliva during intraoral administration. Further, Neuser teaches a coating for the tablet core that comprises an active agent (FF 38). There is no evidence on this record that such a coating would not disintegrate or dissolve within 10 minutes, when the composition is contacted with saliva during intraoral administration.

Accordingly, we are not persuaded by Appellants' argument to the contrary. Therefore, we affirm the rejection of claim 48 under 35 U.S.C

§ 103(a) as unpatentable over the combination of Neuser, Lewis and Liedtke.

Claim 53:

Claim 53 depends from and further limits that the active ingredient in the first intraoral composition of claim 33 to a dosage of between 10 micrograms and 30 mg.

According to Appellants "[t]he examiner has cited no art disclosing the claimed dosage range of one [microgram] to 50 mg, much less the claimed range of 10 [micrograms] to 30 mg of claim 53, for a drug to be delivered intraorally" (App. Br. 20). We disagree, *see* FF 41.

Accordingly, we are not persuaded by Appellants' assertion to the contrary and the rejection of claim 53 under 35 U.S.C § 103(a) as unpatentable over the combination of Neuser, Lewis and Liedtke is affirmed.

Claim 55:

Appellants assert that "[t]he same arguments made with respect to the formulations are equally applicable here" (App. Br. 20.) We are not persuaded. For the reasons set forth above, we were not persuaded by Appellants' arguments regarding the formulation claims. Appellants make no other argument with regard to the Examiner's prima facie case of obviousness. Accordingly we affirm the rejection of claim 55 under 35 U.S.C § 103(a) as unpatentable over the combination of Neuser, Lewis and Liedtke. Claim 56 falls together with claim 55.

9. Claims 33-43 and 49-57 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Barclay and Pather.

Based on the combination of references relied upon the Examiner concludes that

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Barclay et al and [Pather] and utilize the instant amount of prochlorperazine since [Pather] teaches the instant amount of the prochlorperazine is utilized to administer the drug in the mouth. Further, one would have been motivated to utilize an effervescent agent in the buccal region of Barclay's device since [Pather] teaches the use of effervescent agents as penetration enhancers in sublingual/buccal tablets, which facilitates the permeation of the drug across the oral mucosa. Therefore, a skilled artisan would have been motivated to add an effervescent agent to increase the penetration of the drug through the oral mucosa.

(Ans. 14.)

Appellants' claimed invention requires that the first intraoral portion "is a film coating that is applied to the core or a compression coating that is compressed around the core" (Claims 33, 41, and 55). The Examiner has not identified, and we do not find, a teaching in Barclay of a film coating applied to the core or a compression coating that is compressed around the core of the formulation. To the contrary, Barclay teaches a device wherein the active ingredients are disposed inside compartments surrounded by a wall having a passageway there through for the passage of the active agents. Pather fails to make up for this deficiency in Barclay.

Accordingly, we reverse the rejection of claims 33-43 and 49-57 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Barclay and Pather.

Obviousness-type double patenting:

10. Claims 33-57 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of Hirsh 1.

The Examiner finds that "the conflicting claims are not identical, they are not patentably distinct from each other because both applications contain similar subject matter" (Ans. 14 (emphasis removed)). In response, Appellants state that they "will file a terminal disclaimer to overcome the double patenting rejection" (App. Br. 22).

Accordingly, we summarily affirm the rejection of claims 33-57 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of Hirsh 1.

11. Claims 33-57 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of Hirsh 2.

The Examiner finds that "the conflicting claims are not identical, they are not patentably distinct from each other because both applications contain similar subject matter" (Ans. 14 (emphasis removed)). In response, Appellants state that they "will file a terminal disclaimer to overcome the double patenting rejection" (App. Br. 22).

Accordingly, we summarily affirm the rejection of claims 33-57 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of Hirsh 2.

CONCLUSION

In summary, we affirm rejections 2, 4, 5, 8, 10, and 11(as numbered *supra*, pp. 4-5). We reverse rejections 1, 3, 6, 7, and 9 (*id.)*.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

lp

PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE, SUITE 1200
1201 PEACHTREE STREET
ATLANTA GA 30361